April 9, 2004

TO: Division of Dockets Management (HFA-305)
Food and Drug Administration
5360 Fishers Lane, Room 1061
Rockville, MD 20851

FR: Cynthia Pearson, Executive Director
National Women's Health Network

RE: Comments on "Draft Guidance for Industry and FDA Staff on Saline, Silicone Gel, and Alternative Breast Implants" Docket Number 2004D-0002

On behalf of the National Women's Health Network, a consumer advocacy organization devoted to women and health, I am pleased to submit these comments on the Draft Guidance for Industry and FDA Staff on Saline, Silicone Gel, and Alternative Breast Implants.

The Network commends the FDA for several of the changes in the draft guidance that begin to address the concerns that were raised by women during the October 2003 Advisory Panel meetings. It is clear that we still do not have accurate information about rupture rates, gel bleed and gel migration for silicone implants. We support the recommendations that mechanical testing be modified to predict clinical outcomes, sponsors develop new tests that can accurately predict rates of rupture over time and that sponsors develop a new gel bleed test that more closely mimics conditions in the body. These tests may begin to provide answers to the questions that women with concerns about implants need to know.

In several areas highlighted, however, the Network finds that the draft guidance falls short by not requiring sponsors to study and gather information about specific problems associated with implants that women have identified as concerns.

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1) In section 9.1 the draft guidance states that "Depending on the data, 2 years of premarket clinical data may not be sufficient to evaluate the safety and effectiveness of your device," and "..additional years of follow-up may be recommended for silicone-gel filled breast implants." The Network recognizes that this is a change in the right direction, but we believe that two years of premarket clinical data is insufficient.

The FDA's own studies show that the median age of rupture for silicone gel-filled implants is 10.8 years (Brown, AJR: 175, October 2000) and that women with extracapsular silicone were more likely to report having fibromyalgia (Brown, The Journal of Rheumatology, 2001; 28:5). Considering that on average women report having problems with implants in years 7-10 post implantation, it is clear that more than two years of clinical data is needed to assess safety and effectiveness of these devices.

Manufacturers have had many opportunities to collect long-term data on implants, yet we still do not have that data. Sponsors are not likely to collect long-term data on implants unless they are required to do so. In addition, due to the FDA's admitted limited authority to enforce postmarket approval requirements, the only way to ensure that long-term safety data is collected is to require it for premarket approval.

The National Women's Health Network recommends that sponsors be directed to conduct premarket clinical trials that collect long-term safety and effectiveness data on breast implants. Sponsors that have had a type of breast implant on the market in other countries should be directed to provide data on those devices, and if this data does not exist sponsors should be directed to conduct retrospective studies in a manner that assures comprehensive assessment, including using medical records and clinical exams.

2) In section 9.3 the draft guidance states that the following information be provided: "the incidence, timing and severity of interference and or difficulties with lactation," and "the incidence, timing and nature of difficulties with pregnancy." This is the same information that sponsors were asked to provide in the most recent breast implant guidance document, and it is not adequate to lay to rest the questions that have been raised about the effects of implants on pregnancy, lactation and children.

The data that Inamed provided during the October 2003 Advisory Panel meeting showed a high rate of lactation complications among the small group of women who attempted to breastfeed after receiving implants. They did not have information, however, about the causes or further health consequences for women or children of these complications.

In addition to data on rates of pregnancy and lactation complications, information is needed on how to evaluate the nature and severity of these problems. Information is

needed about the effects of gel bleed and migration in lactating and pregnant women with silicone gel implants. Women with silicone gel-implants who experience lactation complications should be evaluated with MRI to detect possible rupture or gel migration. Breast milk in lactating women in the study should be tested for the presence of silicone gel. Children born to women post-implantation should receive long-term follow-up, and they should be followed as two groups; those who were breast fed and those who did not breast feed.

3) The data provided by Inamed for its silicone gel-filled implant during the October 2003 Advisory Panel meeting showed a significantly higher reoperation rate for reconstruction patients vs. augmentation patients (46% rate vs. 20% rate up to three years after implantation). This high complication rate is not acceptable.

The draft guidance does recommend that sponsors gather new information on breast cancer patients. The Network supports the recommendation in section 9.2 that sponsors provide a description of cancer treatments on all reconstruction patients and on reconstruction and augmentation patients who develop breast cancer during the course of the study. We also support the recommendation in section 9.3 that sponsors collect information on incidence, timing, and type of new breast cancer diagnosis post-implantation, including mammographic difficulties caused by implants.

However, additional information is needed. To adequately address the concerns of breast cancer patients considering implants, FDA needs to understand why the failure rate for implants is so much higher for reconstruction patients. It also needs to understand whether the effects of silicone gel migration in women who have already experienced cancer might be different, and whether cancer survivors might be more vulnerable to some silicone-related problems.

4) As stated above, the Network supports the enhanced biomaterials testing in the draft guidance which may begin to answer questions about why implants rupture. It is important to understand the circumstances under which implants rupture. But it is also important to understand what happens in a woman's body when implants rupture. Until a rupture-proof implant is developed, companies must be required to collect long-term clinical data that will enhance knowledge about the clinical consequences of untreated silent rupture.